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08/487,701 06/07/95 GRAY

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EXAMINER

MARSCHER, A

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

09/22/99

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

Application No.  
**08/487,701**

Applicant(s)  
**Gray et al.**

Examiner  
**Ardin Marschel**

Group Art Unit  
**1655**



☒ Responsive to communication(s) filed on 11/30/98(Not. of App), 6/30/99(App. Br.), and 8/6/99(Term. Dis.).

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

## Disposition of Claims

☒ Claim(s) 48-69, 71-86, 88-93, and 95-97 is/are pending in the application.

~~of the above~~ Claim(s) 1-47, 70, 87, and 94 have been canceled. ~~is/are withdrawn from consideration~~

☐ Claim(s) \_\_\_\_\_ is/are allowed.

☒ Claim(s) 48-63, 65-69, 71-86, 88-93, and 95-97 is/are rejected.

☒ Claim(s) 64 is/are objected to.

☐ Claims \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

## Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

The art unit designated for this application has changed. Applicant(s) are hereby informed that future correspondence should be directed to Art Unit 1655.

In view of the appeal brief, filed 6/30/99, and terminal disclaimer, filed 8/6/99, and newly found rejections summarized herein, PROSECUTION IS HEREBY REOPENED. New grounds of rejection are set forth below.

To avoid abandonment of the application, appellant must exercise one of the following two options:

file a reply under 37 CFR 1.111; or  
request reinstatement of the appeal.

If reinstatement of the appeal is requested, such request must be accompanied by a supplemental appeal brief, but no new amendments, affidavits (37 CFR 1.130, 1.131, or 1.132) or other evidence are permitted. See 37 CFR 1.93(b)(2).

Applicants' arguments, filed 6/30/99, and terminal disclaimer, filed 8/6/99, have been fully considered and they have overcome the previous rejections of record. Reconsideration of the instant claims, however, has resulted in the below summarized new grounds of rejection. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. The finality

of the office action, mailed 5/29/98, is hereby withdrawn.

If applicant desires priority under 35 U.S.C. § 120 based upon a previously filed copending application, specific reference to the earlier filed application must be made in the instant application. It is noted that this appears as the first sentence of the specification following the title. The status of non-provisional application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. \_\_\_\_\_" should follow the filing date of the parent application. If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application. Applicants are also requested to clarify such amendments regarding continuity by canceling previous paragraphs directed to this which have not been canceled in the past when new paragraphs have been added.

Claims 48-63, 65-69, 71, 72-86, 88, 90-93, 95, and 96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. NEW MATTER in the claims is directed to a complexity of 40 kb as given in claim 48, line 3, for example, plus other claims. Consideration of the support for the instant claims revealed that the closest

disclosure is given in the instant specification on pages 21-22, bridging sentence; page 24, lines 1-5; page 44, lines 6-14, and page 45, lines 1-14. It is noted that all complexities for probes are described as being on the order of 50 kb or greater whereas the 40 kb size is only disclosed regarding a probe length and not its complexity or, alternatively a target length, again without complexity disclosure.

Claims 72-74, 76-86, 88-93, and 95-97 are rejected, as discussed below, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Cited on the enclosed PTO Form 892 is page 418 of the textbook Cell Biology which describes interphase cellular structure as containing a nucleus which is made up of "dispersed chromatin" as shown in the Figure 9-18 as stage 1 and noted in the Figure 9-20 figure legend as "dispersed chromatin characteristic of interphase". Thus, interphase is a cellular stage without condensed and morphologically identifiable chromosomes. The lack of condensed chromosomes prevents the presence of morphologically identifiable chromosomes. Therefore, claims which cite the phrase "morphologically identifiable chromosome" while also requiring the cell as being in interphase is a conflict and causes such claims to be vague and indefinite

due to requiring both interphase chromosomal DNA and identifiable chromosomes. Claim 72, and claims dependent from claim 72 due to their dependence, are vague and indefinite due to requiring these two limitations together in part (b).

Claim 96 is additionally vague and indefinite because it is unclear whether the removal of repetitive segments is a required step for performance of the claim or not. The phrase "have been removed" in line 2 of claim 96 is in the past tense which is interpretable as being a removal step that is performed in the past before the performance of claim 96. Is this removal step required regarding claim 96 or not? Clarification is requested.

Claims 50 and 75 are rejected, as discussed below, under 35 U.S.C. § 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Claim 50 does not further limit claim 48 from which it depends because in-situ hybridization is always performed within a cell nucleus whether the DNA is in a chromosomal form which is morphologically identifiable or, alternatively, within the cell nucleus, for example, during interphase. Thus, claim 50 does not further limit the location of chromosomal DNA as given already in claim 48 from which claim 50 depends. It is additionally noted that consideration of the mitochondrial DNA in eukaryotic cells reveals that it is not chromosomal DNA but rather naked DNA as

stated in the textbook Cell Biology on page 232, lines 23-27, and therefore not a concern regarding this rejection. Claim 75 also contains this issue.

The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 72, 74-86, 88-93, and 95-97 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Weissman et al. (P/N 4,710,465), taken in view of Lichter et al. [PNAS, Vol. 85, pp. 9664-9668 (1988)] (both already of record).

The instant invention is directed to the use of high complexity unique sequence probes for hybridization labeling of chromosomes.

Weissman et al. disclose in columns 5-6, bridging paragraph, that the invention therein described detects chromosomal arrangements such as the spacing between genes including linkage that may be related to a disease. Probed regions are disclosed as 50 kb to 2000 kb in column 9, lines 14-32, which clearly qualifies as high complexity probes as instantly claimed. The coverage of the probed region is accomplished as depicted in Figure 5 (discussed in column 18, lines 32-62) and discussed as to probes prepared in the bridging paragraph between columns 18 and 19. The probes prepared in Weissman et al. are directed to unique segments as described in column 14, line 45, through column 20, line 29, therein described as single-copy segments. Weissman et al. lacks hybridization to interphase targets but is not limited as to target type. Hybridization of probes to metaphase targets are specifically exemplified in EXAMPLE XI in column 31, line 31, through column 32, line 5.

Lichter et al. describes the equivalence of metaphase and interphase target assays for genetic abnormalities in the abstract.

Thus, it would have been obvious to someone of ordinary skill in the art at the time of the instant invention to practice high complexity unique sequence (single-copy) probes and their use in hybridization assay as instantly claimed because Weissman et al. describes the method and the motivation to apply this to chromosomal study and Lichter et al. motivates and suggests the



equivalent of metaphase and interphase chromosomal in-situ hybridization for such chromosomal study thus resulting in the practice of the instant invention.

The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman*, 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 72, 74-86, 88-93, and 95-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 125 of copending application Serial No. 08/473,327. Although the conflicting claims are not identical, they are not patentably distinct from each other because the probe type in said claim 125 is generic with regard to type and unique sequence probes are most commonly the probe type utilized in the hybridization art thus making that specie of probe well known within generic probes types as in said claim 125 thus suggesting and motivating the unique probe type in the instant claim practice. The various

abnormalities of the instant claims are also extremely well known chromosomal abnormalities that are assessed by hybridization assay. It is also noted that the method of said claim 125 starts with staining as the first step and ends with the obvious indicative practice step which is motivated by staining as an obvious step. Otherwise, why stain at all? Lastly the complexity is high in both sets of claims and clearly overlap regarding complexity of probe practice.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 72, 74-86, 88-93, and 95-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 48, and 50-58 of copending application Serial No. 08/477,316. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of staining utilizing unique sequence high complexity probes. The instant claims include any chromosome whereas the specific chromosomes of 08/477,316 are clearly species therein. The various abnormalities of the instant claims are also extremely well known chromosomal abnormalities that are assessed by hybridization assay. Lastly the complexity is high in both sets of claims and clearly overlap

regarding complexity of probe practice.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 72, 74-86, 88-93, and 95-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 48-50 of copending application Serial No. 08/487,387. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of staining utilizing unique sequence high complexity probes. The instant claims include any chromosome whereas the specific chromosomes and well known components therein, such as paracentric regions, of 08/487,387 are clearly species therein. The various abnormalities of the instant claims are also extremely well known chromosomal abnormalities that are assessed by hybridization assay. Lastly the complexity is high in both sets of claims and clearly overlap regarding complexity of probe practice.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 72, 74-86, 88-93, and 95-97 are provisionally rejected under the judicially created doctrine of obviousness-

type double patenting as being unpatentable over claims 62-65 and 125-148 of copending application Serial No. 08/478,740. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of staining utilizing high complexity probes. The instant claims include generic sample sources including fetal DNA which clearly includes specific fetal DNA sample of 08/478,740 as species therein. See the fetal limitation in instant claim 76. The various abnormalities of the instant claims are also extremely well known chromosomal abnormalities that are assessed by hybridization assay. Lastly the complexity is high in both sets of claims and clearly overlap regarding complexity of probe practice.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 72, 74-86, 88-93, and 95-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 18-33 of copending application Serial No. 08/472,312. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of staining utilizing unique sequence high complexity probes. The instant claims include any chromosome whereas the

specific chromosomes of 08/472,312 are clearly species therein. The various abnormalities of the instant claims are also extremely well known chromosomal abnormalities that are assessed by hybridization assay. Lastly the complexity is high in both sets of claims and clearly overlap regarding complexity of probe practice.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 72, 74-86, 88-93, and 95-97 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 131, 132, 144-147, and 150-153 of copending application Serial No. 08/487,974. Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are directed to methods of staining utilizing unique sequence high complexity probes. The instant claims include any chromosome whereas the specific fluorescent labeling of 08/487,974 are clearly species therein. The various abnormalities of the instant claims are also extremely well known chromosomal abnormalities that are assessed by hybridization assay. Lastly the complexity is high in both sets of claims and clearly overlap regarding complexity of probe practice.

This is a *provisional* obviousness-type double patenting

rejection because the conflicting claims have not in fact been patented.

Claim 64 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

No claim is allowed.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The CM1 Fax Center number is either (703) 308-4242 or (703) 305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ardin Marschel, Ph.D., whose telephone number is (703) 308-3894. The examiner can normally be reached on Monday-Friday from 8 A.M. to 4 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

September 21, 1999

*Ardin H. Marschel*  
ARDIN H. MARSCHEL  
PRIMARY EXAMINER